

Applicants: Irene Mary Horne et al.  
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In the Specification

Please amend the paragraph on page 3, line 30 though page 4, line 9, as follows:

In a first aspect the present invention provides a recombinant polynucleotide, the polynucleotide comprising a first and a second sequence, the first sequence encoding a signal peptide comprising a TAT signal and a Sec avoidance signal and the second sequence encoding a heterologous protein, wherein the sequence of the signal peptide is

M-X<sub>1</sub>-K/R-X<sub>2</sub>-K/R-X<sub>3</sub>-RR-X<sub>4</sub>-K/R-A (SEQ ID NO: 41)

in which X<sub>1</sub> is a sequence of 0 to 10 amino acids;  
X<sub>2</sub> is a sequence of 0 to 3 amino acids;  
X<sub>3</sub> is a sequence of 0 to 10 amino acids; and  
X<sub>4</sub> is a sequence of 15 to 24 amino acids in which at least 75% up to about 90% of the residues are hydrophobic.

Please amend the paragraph on page 4, lines 10-17, as follows:

In a second aspect the present invention provides a signal peptide, the signal peptide having the sequence

M-X<sub>1</sub>-K/R-X<sub>2</sub>-K/R-X<sub>3</sub>-RR-X<sub>4</sub>-K/R-A (SEQ ID NO: 41)

in which X<sub>1</sub> is a sequence of 0 to 10 amino acids;  
X<sub>2</sub> is a sequence of 0 to 3 amino acids;  
X<sub>3</sub> is a sequence of 0 to 10 amino acids; and  
X<sub>4</sub> is a sequence of 15 to 24 amino acids in which at least 75% up to about 90% of the residues are hydrophobic.

Please amend the paragraph on page 4, line 18 through page 5, line 8, as follows:

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In a third aspect the present invention provides a method of producing a heterologous polypeptide from a host cell comprising a TAT translocation system, the method comprising:

(i) transforming the host cell with a DNA sequence encoding the heterologous polypeptide and a signal peptide wherein the signal peptide comprises a TAT signal and a Sec avoidance signal wherein the sequence of the signal peptide is

M-X<sub>1</sub>-K/R-X<sub>2</sub>-K/R-X<sub>3</sub>-RR-X<sub>4</sub>-K/R-A (SEQ ID NO: 41)

in which X<sub>1</sub> is a sequence of 0 to 10 amino acids;  
X<sub>2</sub> is a sequence of 0 to 3 amino acids;  
X<sub>3</sub> is a sequence of 0 to 10 amino acids; and  
X<sub>4</sub> is a sequence of 15 to 24 amino acids in which at least 75% up to about 90% of the residues are hydrophobic.

(ii) culturing the host cell under conditions which allow expression of the heterologous polypeptide; and  
  
(iii) recovering the heterologous polypeptide secreted from the host cell via the TAT translocation system.

Please amend the paragraph on page 5, line 26 though page 6, line 8, as follows:

Accordingly, in a first aspect the present invention provides a recombinant polynucleotide, the polynucleotide comprising a first and a second sequence, the first sequence encoding a signal peptide comprising a TAT signal and a Sec avoidance signal and the second sequence encoding a heterologous protein, wherein the sequence of the signal peptide is

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M-X<sub>1</sub>-K/R-X<sub>2</sub>-K/R-X<sub>3</sub>-RR-X<sub>4</sub>-K/R-A (SEQ ID NO: 41)

in which X<sub>1</sub> is a sequence of 0 to 10 amino acids;  
X<sub>2</sub> is a sequence of 0 to 3 amino acids;  
X<sub>3</sub> is a sequence of 0 to 10 amino acids; and  
X<sub>4</sub> is a sequence of 15 to 24 amino acids in which at least 75% up to about 90% of the residues are hydrophobic.

Please amend the paragraph on page 6, lines 9-16, as follows:

In a second aspect the present invention provides a signal peptide, the signal peptide having the sequence

M-X<sub>1</sub>-K/R-X<sub>2</sub>-K/R-X<sub>3</sub>-RR-X<sub>4</sub>-K/R-A (SEQ ID NO: 41)

in which X<sub>1</sub> is a sequence of 0 to 10 amino acids;  
X<sub>2</sub> is a sequence of 0 to 3 amino acids;  
X<sub>3</sub> is a sequence of 0 to 10 amino acids; and  
X<sub>4</sub> is a sequence of 15 to 24 amino acids in which at least 75% up to about 90% of the residues are hydrophobic.

Please amend the paragraph on page 6, line 17 through page 7, line 7, as follows:

In a third aspect the present invention provides a method of producing a heterologous polypeptide from a host cell comprising a TAT translocation system, the method comprising:

(i) transforming the host cell with a DNA sequence encoding the heterologous polypeptide and a signal peptide wherein the signal peptide comprises a TAT signal and a Sec avoidance signal wherein the sequence of the signal peptide

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is

M-X<sub>1</sub>-K/R-X<sub>2</sub>-K/R-X<sub>3</sub>-RR-X<sub>4</sub>-K/R-A (SEQ ID NO: 41)

in which X<sub>1</sub> is a sequence of 0 to 10 amino acids;  
X<sub>2</sub> is a sequence of 0 to 3 amino acids;  
X<sub>3</sub> is a sequence of 0 to 10 amino acids; and  
X<sub>4</sub> is a sequence of 15 to 24 amino acids in which at least 75% up to about 90% of the residues are hydrophobic.

- (ii) culturing the host cell under conditions which allow expression of the heterologous polypeptide; and
- (iii) recovering the heterologous polypeptide secreted from the host cell via the TAT translocation system.

Please amend the paragraph on page 30, lines 6-16, as follows:

The present invention provides a recombinant polynucleotide, the polynucleotide comprising a first and a second sequence, the first sequence encoding a signal peptide comprising a TAT signal and a Sec avoidance signal and the second sequence encoding a heterologous protein. The sequence of the signal peptide is M-X<sub>1</sub>-K/R-X<sub>2</sub>-K/R-X<sub>3</sub>-RR-X<sub>4</sub>-K/R-A (SEQ ID NO: 41) in which X<sub>1</sub> is a sequence of 0 to 10 amino acids, X<sub>2</sub> is a sequence of 0 to 3 amino acids, X<sub>3</sub> is a sequence of 0 to 10 amino acids and X<sub>4</sub> is a sequence of 15 to 24 amino acids in which at least 75% up to about 90% of the residues are hydrophobic.